References.

Boudin: Annal. d'Hyg., Paris, Jan., 1861. 2nd s., vol. 15, p. 17.

Goldberger, J., Wheeler, G. A., and Sydenstricker, E., A Study of the Diet of Non-pellagrous and of Pellagrous Households: J. Am. Med. Assn., Sept. 21, 1918, vol. 71, pp. 944–949.

———, A Study of the Relation of Diet to Pellagra Incidence in Seven Textile-Mill Communities of South Carolina in 1916: Public Health Reports, Washington, D. C., March 19, 1920, vol. 35, pp. 648–713.

Siler, J., Garrison, P. E., and MacNeal, W. J., Statistics of Pellagra in Spartanburg County, etc.: Arch. Int. Med., Jan., 1915, vol. 15, p. 98.

Sydenstricker, E., Wheeler, G. A., and Goldberger, J., Disabling Sickness Among the Population of Seven Cotton-Mill Villages of South Carolina In Relation to Family Income: Public Health Reports, Washington, D. C., Nov. 22, 1918, vol. 33, pp. 2038–2051.

CAN THE MOSQUITO CONVEY INFECTION FROM A MALARIA PATIENT UNDERGOING TREATMENT?—DOES SPOROGONY AFFECT MOSQUITO LIFE?

By BRUCE MAYNE, Biologist, United States Public Health Service.

It is possibly of more than academic interest to consider the effect quinine exerts on the mature gametocyte when it is taken up and elaborated in the mosquito. Information on this matter would probably be of some value in determining how soon after beginning treatment a malaria patient is no longer a source of infection for mosquitoes, and it has a practical bearing on the problem of the necessity of isolating the patient by screening.

We know that although every case of malaria is a potential medium for the production of gametocytes, these sexual bodies do not develop until the malarial infection has persisted for several days—8 to 15 days in the case of subtertian malaria, and 7 to 10 days in tertian and quartan malaria—following the onset of definite symptoms of infection. We must appreciate the fact that the infection may be present for a considerable time before the patient gives tangible evidence of its occurrence, so that gametocyte production may be fairly started and the actual time required for the development of gametes may be longer than is generally accounted. It is even possible that the blood may contain at least partially grown parasites before distinct symptoms of malarial infection are noted. This is especially true of latent malaria, and often in these cases the patient harboring moderate numbers of plasmodia not only does not exhibit symptoms but is performing severe manual labor.

Several authorities have reported that after the gametes of the various types of plasmodia have reached maturity, quinine is ineffective in action so far as their development within the mosquito

is concerned. Barber (1918) [1] has indicated in his mosquito-infectivity experiments that quinine apparently has little effect on gametes further than to increase the rate of their disappearance. In numerous trials this worker has shown that human carriers were capable of infecting mosquitoes when quinine was administered in curative doses.

In commenting on the effect of quinine on the malaria parasite in the mosquito, Darling (1910) [2] states, relative to his researches: "Nearly all the infecting experiments were conducted on patients who were receiving the routine ward treatment of quinine sulphate, grains 10, thrice daily in solution, so that, apparently, quinine in these quantities has no destructive or inhibitive effect on the parasites in the mosquito because the zygotes go on to maturity and sporozoites (*P. falciparum*) appear in the salivary glands in from 9 to 11½ days."

Ross (1910),[3] reviewing the literature relative to infectivity, states: "An important point in connection with the prevention of malaria is that Bignami and Bastianelli, Gualdi and Martirano, and Schaudinn have succeeded in infecting anophelines from patients who had been taking quinine. Schaudinn's case had been taking 1 gram thrice a week. Ziemann regards this as indicative that the male gametids are not destroyed as he thought. It also suggests that cases of crescents are likely to prove sources of infection in spite of energetic treatment."

Loeffler (1905),[4] discussing at length the question, Will malaria parasites develop in a mosquito which has bitten a person under quinine treatment? remarks: "The action of quinine on the gametocyte must be a paramount consideration before considering the effect on the insect imbibing quinine-treated blood. When it is observed that crescents can not be caused to disappear from the blood even by long-continued use of massive doses of quinine, the carrier problem from the public-health viewpoint becomes more acute; and if it be determined that the subsequent development of these forms in the stomach of the mosquito can not be prevented under quinine treatment, the sanitary significance of the human-carrier problem becomes more serious.

"Gualdi and Martirano have administered large doses of quinine to patients that had crescents, and after having satisfied themselves by an examination of the urine that the quinine had been actually absorbed, they caused numerous anopheles that had been reared in

[1] M. Barber (1918), Some observations and experiments on Malayan Anopheles with special reference to the transmission of malaria: The Philippine Journal of Science, vol. 13, sec. B, No. 1, p. 23.

[2] S. T. Darling (1910), Studies in relation to malaria: Isthmian Canal Commission Bulletin, p. 32, Washington.

[3] R. Ross (1910), Prevention of Malaria, p. 137, John Murray, London.

[4] F. Loeffler (1905), Malaria Diseases: Modern clinical medicine, p. 291, D. Appleton Co., New York.

the laboratory to suck the blood of these patients. A considerable percentage of these mosquitoes were found to be infected a few days later. On the other hand, in an experiment with tertian malaria, Schoo, in Holland, concludes that in tertian fever not only the asexual forms are destroyed by quinine but also the gametes, and that a single dose of 1 gram quinine sulphate is sufficient to prevent development of gametes in the mosquito. The details are given as follows: A patient who had infected large numbers of anophelines was given 1 gram of quinine sulphate and during three days was bitten by 16 specimens of anophelines. No infections resulted.

"In another experiment a patient with tertian malaria was bitten by 10 anophelines during an untreated period. Six hours after a gram of quinine sulphate was administered, he was bitten by 9 anophelines. Eight specimens of the former lot were found infected during 12 days incubation. None of the latter lot was found infected."

This latter observation is directly in agreement with the writer's experience with the attempted conveyance of the parasites of tertian malaria. We must take into account in order to interpret results with *P. vivax*, that—

1. Fewer gametocytes are required to infect a mosquito. In comparison with the law of infectivity established by Darling, that the probable minimum number of gametocytes of *P. falciparum* necessary to infect a mosquito is 1 to 500 leucocytes, I have found that in blood containing 1 gametocyte of *P. vivax* to 650 leucocytes, infectivity resulted.

2. Gametocytes of *P. vivax* are, to be sure, much less resistant to the action of quinine than are the gametocytes of *P. falciparum*, so that less quinine is required to inhibit mosquito infectivity.

It is evident that when no change occurs in the morphology of the fully developed gametocyte in the presence of quinine, the development within the mosquito is not impaired by the drug. This has been shown in experiments conducted in New Orleans and in the works of Darling and of the Italians. In the Canal Zone reports, the conclusion is drawn by Darling that mosquitoes may become infected from blood of patients who had been previously given as high as 450 grains of quinine. In experiments conducted in the United States Public Health Service malaria laboratory in Memphis, Tenn., this observation was carried a step further in proving that such mosquitoes not only harbored typical sporonts, showing that quinine did not alter the morphology or viability of the parasites, but also communicated the infection when induced to bite a healthy volunteer. The patient in this experiment had received 400 grains of quinine sulphate before attempting to infect the mosquito (*A. quadrimaculatus*), and 80 grains were added during the interval of applying the mosquito in the two blood meals. Two weeks fol-

lowing the administration of the 480 grains of quinine, the mosquito was allowed to bite the healthy contact, and in the course of 11 days acute symptoms of the disease were recorded in the new host. A microscopical confirmation of the presence of the parasites (*P. falciparum*) was obtained.

The apparent ease with which sporozoites are killed when introduced into blood protected by quinine in attempted human prophylaxis is contrasted with the survival of the gametocytes taken up by the mosquito from blood treated with quinine.

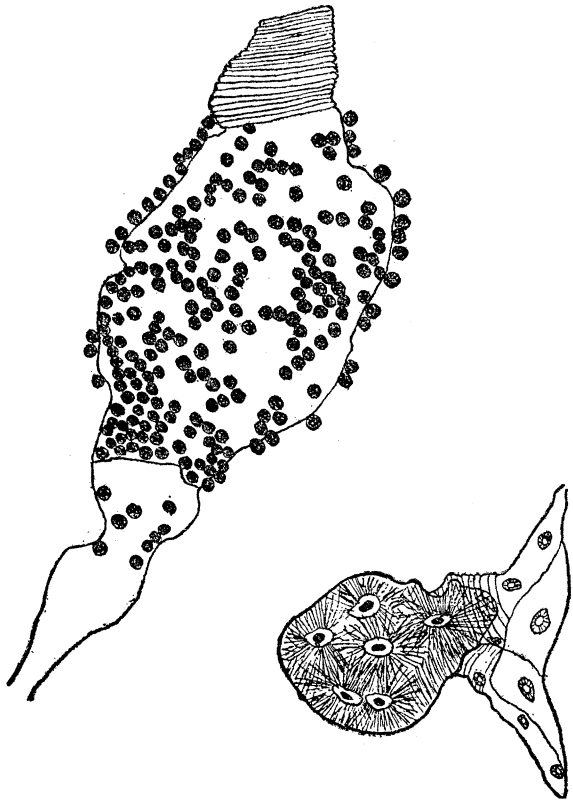

FIG. 1.—The appearance of a mosquito stomach heavily infested with oocysts—15 days incubation. (Camera lucida drawing.)

FIG. 2.—An oocyst selected from the stomach wall, showing manner of extrusion through the gut epithelium

Relative to the longevity of the mosquito host influenced by malaria infection, it must be pointed out that, as far as our observations carry us, no physiological disturbances are indicated. I believe that this is generally accepted relative to the invasion of the alimentary tract of any insect by the human protozoan parasites. We have observed mosquito stomachs studded with tumor-like masses of

oocysts in advanced stages of sporogony. As many as 250 have been counted and up to 400 estimated. It is recalled that these bodies have developed after having actually penetrated the wall of the mid-gut and becoming encysted prior to bursting their capsules and, in the form of sporozoites, forcibly invading the salivary glands. The extent of rupturing of the tissues can be appreciated in sections of the gut epithelium, where all stages of the process have been observed. Figure 1 illustrates typical parasitism on the insect's stomach, and Figure 2 the manner of extrusion of a single oocyst through the gut wall.

In specimens in which the oocysts have discharged their contents and nothing remains but the enveloping capsules, the damage committed is not appreciable. I believe that if the individual mosquito had not been made to meet an untimely death for the purpose of dissection, it probably would have lived its normal life. In this connection it may be of interest to note that under laboratory experimentation mosquitoes have survived infection for unusually long periods. A French writer, Roubaud (1918),[1] working in France with *A. quadrimaculatus* and *P. falciparum*, found that mosquitoes survived parasitism under laboratory conditions for as long as 125 days. In this instance a dissected specimen revealed a few dead sporozoites in one of its salivary glands.

Under similar conditions the writer has succeeded in keeping mosquitoes alive for over six months. A specimen of *A. punctipennis* survived to the age of 185 days on being fed occasionally on fruit juice, mainly that of raisins and dates. Another specimen of this species, fed on a patient harboring *P. vivax*, was found to retain a few scattered degenerate-appearing sporozoites in two lobes of its salivary glands for a period of 158 days. These organisms were presumably dead, without motility and lacking definite nucleus. The pandemicity of malarial fever may, in no small measure, be accounted for by the longevity of the insect host, associated with its resistance to protozoan invasion.

We are furnished a contrast in the dissemination of filariasis by its insect hosts and are led to speculate on one of the causes contributing to the limitation of the spread of this disease. It is due, possibly, to the relatively high mortality of mosquitoes fed on blood containing microfilarial parasites. The invading parasite penetrates the mosquito's stomach wall, following the forcible rupturing of the enveloping sheath of the worm. In a short time the thoracic muscles in the mosquito are torn by the migrating embryo, followed by the ejection of the developed Filaria through Dutton's membrane of the mosquito's proboscis. The extent of trauma sustained would be

[1] E Roubaud (1918), Recherches sur la transmission du paludisme par les anopheles francais de régions non palustres: Ann. Inst. Pasteur, vol. 32, No. 9, pp. 430–462.

sufficient, I believe, to account for the premature death of the parasitized insect host. In this connection, Bahr (1912)[1] notes that the developing Filaria has a deleterious effect on the health of the mosquito. Heavily infected mosquitoes can be readily recognized by their attitude and general appearance. The intermediate insect host is observed to become more and more sluggish until, ultimately, it is unable to insert its stilettes. In Bahr's experiments it is recorded that about 95 per cent of mosquitoes fed on light infections of filariasis survived until the twenty-first day, and less than 9 per cent of those fed on heavily infected patients lived until the twenty-first day. In comparison with protozoan infection of anophelines, *Stegomyia calopus*, which survives to the age of 154 days, was observed to harbor microfilariæ a maximum of 17 days.

DIVISION OF VENEREAL DISEASES, MAY, 1920.

During the month of May, 1920, 23,101 cases of venereal diseases were reported to the State boards of health by physicians, hospital superintendents, clinicians, etc., as is shown by the accompanying table. The table also shows that there were 9,498 new admissions to the clinics operating under the joint control of the United States Public Health Service and the State boards of health.

Five States have not submitted reports.

Venereal disease reports for May, 1920: Number of cases reported by the State boards of health, number of admissions to the venereal disease clinics operating under joint control of United States Public Health Service and State boards of health, and number of treatments of arsphenamine administered.

State.	Cases reported.				Admissions to clinics.				Arsphenamine treatments administered.
	Total cases.	Gonorrhea.	Syphilis.	Chancroid.	Total admissions.	Gonorrhea.	Syphilis.	Chancroid.	
Alabama	1,208	522	648	38	721	257	443	21	1,654
Arizona	50	31	19	.....	5	.....	5	.....	14
Arkansas	410	219	168	23	159	77	74	8	367
California	371	165	206	.....	245	103	142	.....	1,028
Colorado	593	169	414	10	121	65	53	3	223
Connecticut	271	99	172	.....	86	52	33	1	280
Delaware [2]	.....	.....	.....	.....	.....	.....	.....	.....	.....
Florida	247	103	136	8	317	98	219	.....	1,066
Georgia	1,132	645	438	49	388	235	135	18	1,601
Idaho	31	20	11	.....	.....	.....	.....	.....	.....
Illinois	3,421	1,728	1,622	71	463	214	234	15	1,855
Indiana	583	298	270	15	554	288	238	28	1,992
Iowa	282	177	95	10	108	59	48	1	372
Kansas	441	234	202	5	231	119	106	6	525
Kentucky	402	179	213	10	160	75	85	.....	705
Louisiana	451	238	164	49	357	167	139	51	622
Maine [2]	.....	.....	.....	.....	.....	.....	.....	.....	.....
Maryland	404	135	254	15	169	85	69	15	390
Massachusetts	869	615	254	.....	535	240	295	.....	1,900
Michigan	1,802	939	845	18	93	41	49	3	157
Minnesota	908	503	392	13	126	63	62	1	675

[1] P. H. Bahr (1912), Filariasis and elephantiasis in Fiji: Journal London School of Tropical Medicine. Supp. No. 1, pp. 25-26.

[2] Report not submitted.